## AMENDMENTS TO THE SPECIFICATION:

Insert the sequence listing submitted with the concurrently filed Statement under 37 C.F.R. §§ 1.821-1.825 at the end of the specification.

Amend the paragraph beginning on page 10, line 6, as follows.

In another aspect, the invention features an isolated nucleic acid encoding a Death Inducer with SAP Domain amino acid sequence, where this Death Inducer with SAP Domain amino acid sequence is at least 30% identical to the amino acid sequence of SEQ ID NO:2 SEQ ID NO:33 or SEQ ID NO:4 SEQ ID NO:35 and induces DNA condensation and apoptosis in a mammalian cell. However, this Death Inducer with SAP Domain amino acid sequence may also include the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:4 SEQ ID NO:35. In addition, the nucleic acid encoding the Death Inducer with SAP Domain amino acid may include the nucleic acid sequence of SEQ ID NO:1 SEQ ID NO:32 or SEQ ID NO:3 SEQ ID NO:34.

Amend the paragraph beginning on page 10, line 15, as follows.

In yet another aspect, the invention features a method of killing an abnormally proliferating cell. This method involves contacting the abnormally proliferating cell with a *Death Inducer with SAP Domain* nucleic acid sequence, where this contacting results in the expression of a DIS polypeptide in the abnormally proliferating cell. The *Death Inducer with SAP Domain* nucleic acid sequence may include, for example, the nucleic acid sequence of SEQ ID NO:3 SEQ ID NO:34. In

addition, the abnormally proliferating cell may be an endometrial, prostate, or ovarian cell.

Amend the paragraph beginning on page 11, line 12, as follows.

In yet another aspect, the invention features a method of decreasing virus, for example, tumor virus, replication and dissemination. This method includes the step of contacting a cell infected with a virus with a T-HR mutant target gene nucleic acid sequence, where this contacting results in the expression of a T-HR mutant target gene encoded polypeptide in the cell infected with the virus and prevents the virus from replicating and disseminating, or, for instance, from replicating or disseminating. For example, the virus may be a DNA tumor virus. In addition, in desirable embodiments, the T-HR mutant target gene nucleic acid sequence may be a *Taz*, a *GAP SH3 binding* protein, a nucleolin, a Vesicle Associated Protein 1, or a Death Inducer with SAP Domain nucleic acid sequence of SEQ ID NO:3 SEQ ID NO:32 or SEQ ID NO:34.

Amend the paragraph beginning on page 22, line 14, as follows.

By a "DIS nucleic acid sequence" or "Death Inducer with SAP domain nucleic acid sequence," as used herein is meant a nucleic acid sequence that is at least 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identical to a nucleic acid sequence provided of SEQ ID NO:1 SEQ ID NO:32 or SEQ ID NO:3 SEQ ID NO:34 over a region comprising at least 200, 300, 500, 750, 1000, 1500, 2000, 2500, 3000, or 3500 contiguous

nucleotides. In addition, a "DIS nucleic acid sequence" may be identical to the nucleic acid sequence of SEQ ID NO:1 SEQ ID NO:32 or SEQ ID NO:3 SEQ ID NO:34. In desirable embodiments, a "DIS nucleic acid sequence" is a human or a mouse DIS nucleic acid sequence that is at least 75%, 80%, 85%, 90%, or 95% identical to the human DIS nucleic acid sequence of SEQ ID NO:3 SEQ ID NO:34, or to the murine DIS nucleic acid sequence of SEQ ID NO:32, over a region encompassing at least 1000, 2000, 3000, or 3500 contiguous nucleotides, and encodes a protein which induces DNA condensation and apoptosis in mammalian cells.

Amend the paragraph beginning on page 22, line 27, as follows.

By a "DIS polypeptide," a "Death Inducer with SAP domain polypeptide," a "DIS amino acid sequence," or a "Death Inducer with SAP domain amino acid sequence," as used herein is meant an amino acid sequence that is at least 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identical to the amino acid sequence of SEQ ID NO:33 or SEQ ID NO:4 SEQ ID NO:35 over a region comprising at least 50, 75, 100, 200, 300, 500, 700, 900, or 1200 contiguous amino acids. In addition, a "DIS polypeptide" may be identical to the amino acid sequence of SEQ ID NO: 2 SEQ ID NO:33 or SEQ ID NO: 4 SEQ ID NO:35. In desirable embodiments, a "Death Inducer with SAP domain (DIS) polypeptide" or a "Death Inducer with SAP domain (DIS) amino acid sequence" is a human or a mouse DIS polypeptide or amino acid sequence that is at least 30%, 50%, 60%, 70%, 80%, 90%, or 95% identical to the human DIS amino acid sequence of SEQ ID NO:4 SEQ ID NO:35, or the mouse DIS amino acid sequence of

SEQ ID NO: 2 SEQ ID NO:33, over a region encompassing 500, 700, 900, or 1200 contiguous amino acids, and induces DNA condensation and apoptosis in mammalian cells.

Amend the paragraph beginning on page 30, line 14, as follows.

Fig. 2A is sequence comparison between a region of the wild-type and TMD25 polyoma virus large T antigen nucleic acid and amino acid sequences and shows the 20 bp sequence duplication responsible for the TMD25 mutation (SEQ ID NOS:9-12).

Amend the paragraph beginning on page 30, line 21, as follows.

Fig. 2C is a series of large T antigen amino acid sequences and shows the deletion analysis of the TMD25 mutant (SEQ ID NOS:13-21).

Amend the paragraph beginning on page 32, line 22, as follows.

Fig. 22Figs. 22A-22E is are the sense (SEQ ID NO:1 SEQ ID NO:32) and the antisense strand of the murine DIS nucleic acid sequence as well as the corresponding amino acid sequence (SEQ ID NO:2 SEQ ID NOS:33 and 36-45).

Amend the paragraph beginning on page 32, line 25, as follows.

Fig. 23Figs. 23A and 23B is are the murine DIS nucleic acid sequence (SEQ ID NO: 1 SEQ ID NO:32).

Amend the paragraph beginning on page 32, line 26, as follows.

Fig. 24Figs. 24A-24E is are the murine DIS nucleic acid sequence (SEQ ID NO: 1 SEQ ID NO:32) and the amino acid sequence encoded by the open reading frame of murine DIS (SEQ ID NO: 2 SEQ ID NO:33).

Amend the paragraph beginning on page 33, line 1, as follows.

Fig. 25Figs. 25A-25E is are the sense (SEQ ID NO: 3 SEQ ID NO:34) and the antisense strand human DIS nucleic acid sequence as well as the corresponding amino acid sequence (SEQ ID NO:4 SEQ ID NOS:35 and 46-53).

Amend the paragraph beginning on page 33, line 4, as follows.

Fig. 26Figs. 26A and 26B is are the human DIS nucleic acid sequence (SEQ-ID NO: 3-SEQ ID NO:34).

Amend the paragraph beginning on page 33, line 5, as follows.

Fig. 27Figs. 27A-27D is are the human DIS nucleic acid sequence (SEQ ID NO: 3 SEQ ID NO: 34) and the amino acid sequence encoded by the open reading frame of human DIS (SEQ ID NO: 4 SEQ ID NO: 35).

Amend the paragraph beginning on page 33, line 16, as follows.

Fig. 32Figs. 32A and 32B is are a series of Western blots showing that DIS,

PARP, and LaminB are cleaved in BMK and HeLa cells upon induction of apoptosis by

staurosporine (A), and that caspase-3 and caspase-8 inhibitors can inhibit DIS cleavage (B).

Amend the paragraph beginning on page 47, line 27, as follows.

Furthermore, when we induced apoptosis in BMK and HeLa cells with staurosporine, we observed that DIS was degraded and that PARP and LaminB were cleaved (Fig. 32, panel A). Both PARP and LaminB are cleaved by caspases during apoptosis. We also observed that caspase-3 and caspase-8 inhibitors inhibited cleavage of DIS (Fig. 32, panel B). In view of these results, we analyzed the structure of human and mouse DIS and identified a number of caspase-3 and caspase-8 cleavage sites (Fig. 33). *In vitro* caspase cleavage experiments showed that DIS is sensitive to caspase-3 and that the first caspase-3 site (at amino acid 691 in human DIS (SEQ ID NO: 4 SEQ ID NO: 35) and amino acid 689 in murine DIS (SEQ ID NO: 2 SEQ ID NO: 33)) is used for cleavage (Fig. 34). Consequently, DIS is likely to function in regulating apoptosis and may be used in methods to diagnose and treat proliferative disorders.

Amend the paragraph beginning on page 71, line 23, as follows.

We generated TAZ knock out mice by replacing exon 2 (which encodes amino acids 1-144 of murine DIS; SEQ ID NO: 2 SEQ ID NO:33) of the mouse TAZ gene with the pSAbeta-galpGKneopGKdta positive-negative selection vector (Figure 35). The TAZ knock out construct was transfected into an Embryonic Stem (ES) cell line and two positive ES clones were obtained and confirmed by PCR and by Southern blot. A

Southern blot for the *neo* gene also confirmed that only exon 2 of TAZ was replaced. We performed microinjections with these ES clones and obtained chimeric mice. Nine F1 TAZ<sup>+/-</sup> mice were obtained from different chimeric mice and these mice were mated to each other to generate TAZ<sup>-/-</sup> knockout mice.

Amend the paragraph beginning on page 101, line 25, as follows.

Total RNAs from SK-Vector and SK-P150 clones were amplified using primer pairs (5'-CGT CAC CTG AGG TGA CAC AGC AAA GC-3' (SEQ ID NO:22) and 5'-CGC TTC CAG GAC TGC AGG CTT CCT G-3' (SEQ ID NO:23). G3PDH was amplified using (5'-CAG ACC CCA AAT CTG CAG ATA CTC AG-3' (SEQ ID NO:24) and 5'-CAC TGG AAT TGG AAC TCT TCT GTC GAG-3' (SEQ ID NO:25)). Amplification mixtures from cycle numbers with linear amplification were used for comparing relative quantities of transcripts. Amplified G3PDH cDNA was used as an internal control to normalize the amount of p21 cDNA. The ratio of p21 versus G3PDH is the average of three linear amplification cycles.

Amend the paragraph beginning on page 102, line 22, as follows.

ChIP was performed as described previously by Weinmann et al., Methods 26:37-47, 2003). P19 cells extracts were used for ChIP. Chromatin elute was amplified using mouse p21 promoter specific primers: 5'-GAA GTA GGA GTC ACC GTC CTG TTT ACC-3' (SEQ ID NO:26) and 5'-GAT GTC TCT GTA TAG CCC TGG CTG TC-3' (SEQ ID NO:27) for 45 cycles. As a non-specific control, GAPD (glyceraldehyde-3-

phosphate dehydrogenase) gene was amplified with 5'-GCT GAA CGG GAA GCT CAC TGG CAT GG-3' (SEQ ID NO:28) and 5'-GAG GTC CAC CAC CCT GTT GCT GTA GC-3' (SEQ ID NO:29).

Amend the paragraph beginning on page 103, line 2, as follows.

Two p150 specific siRNA duplexes were made (Dharmacon Research, CO) 5'-AAG GAG AUG GAC AGU AAU GAG-3' (SEQ ID NO:30) and 5'-AAC CCC AUU ACC UCC AGA AUC-3' (SEQ ID NO:31) and transfected together into HOSE cells using Oligofectamine (Invitrogen) follow manufacturer's suggestions. The cells were serum-starved (0.2% serum) for 48 hrs and stimulated with 10% FBS and 100 uM BrdU. After 18hrs, cells were fixed and stained for BrdU and DAPI. p21 was detected by immunoprecipitation followed by Western blot. P150 and tubulin were detected directly by Western blot.